outcomes with low local recurrence rate, low rate of progression to NU and renal function preservation are the benefits.

MP5-8.
HISTONE DEACETYLASE INHIBITOR TRICHOSTATIN A SYNERGISTICALLY RESENSITIZES A GEMCITABINE RESISTANT UROTHELIAL CARCINOMA CELLS VIA SUPPRESSION OF TG-INTERACTING FACTOR AND AKT ACTIVATION

Bi-Wen Yeh [1,2], Wei-Ming Li [1,2,3,*], Ching-Chia Li [1,2,4], Wan-Yi Kang [5], Chun-Nung Huang [1,2], Tzyh-Chyuan Hour [6], Zi-Miao Liu [7], Huei-Sheng Huang [7,*], Wen-Jeng Wu [1,2,8,*]. [1] *Department of Urology, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan;* [2] *Department of Urology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan;* [3] *Department of Urology, Ministry of Health and Welfare Pingtung Hospital, Pingtung, Taiwan;* [4] *Department of Urology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan;* [5] *Department of Pathology, Kuo General Hospital, Tainan 701, Taiwan;* [6] *Institute of Biochemistry, Kaohsiung Medical University, Kaohsiung, Taiwan;* [6] *Department of Medical Laboratory Science and Biotechnology, College of Medicine, National Cheng Kung University, Tainan 701, Taiwan;* [8] *Department of Urology, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan*

Purpose: Gemcitabine and cisplatin (GC) has been widely used for advanced and metastatic urothelial carcinoma (UC). However, resistance to this remedy has been noticed. We have demonstrated that increase of TG-interacting factor (TGIF) in specimens is associated with worse prognosis of upper tract UC (UTUC) patients. The roles of TGIF in the gemcitabine resistance of UTUC and a promising therapeutic strategy to UC were explored.
Materials and methods: Specimens of 23 UTUC patients who received GC systemic chemotherapy were collected to evaluate the alterations of TGIF in the resistance to the remedy by using immunohistochemistry. *In vitro* characterizations of mechanisms mediating TGIF in gemcitabine resistance were conducted by analyzing NTUB1 cells and their gemcitabine-resistant sublines, NGR cells.
Results and conclusions: Increased TGIF and p-AKT^{Ser473} are significantly associated with chemo-resistance, poor progression-free survival, and higher cancer-related deaths of UTUC patients. Higher increases of TGIF, p-AKT^{Ser473}, and invasive ability were demonstrated in NGR cells. Overexpression of TGIF in NTUB1 cells upregulated p-AKT^{Ser473} activation, migration ability, and attenuated cellular sensitivity to gemcitabine. Knockdown of TGIF in NGR cells downregulated p-AKT^{Ser473} activation, migration ability, and enhanced cellular sensitivity to gemcitabine. In addition, histone deacetylases inhibitor trichostatin A (TSA) can inhibit TGIF, p-AKT^{Ser473} expression and migration ability. Synergistic effects of gemcitabine and TSA on NGR cells were also demonstrated. Collectively, TGIF contributes to the gemcitabine resistance of UTUC via AKT activation. Combined treatment with gemcitabine and TSA might be a promising therapeutic remedy to improve the gemcitabine resistance of UC.

MP5-9.
OVEREXPRESSION OF HEPATOMA-DERIVED GROWTH FACTOR (HDGF) IS ASSOCIATED WITH WORSE PROGNOSIS IN UPPER URINARY TRACT UROTHELIAL CARCINOMA

Bi-Wen Yeh [1,2], Wei-Ming Li [1,2,3,*], Ming-Hong Tai [4], Ching-Chia Li [1,2,5], Chun-Nung Huang [1,2], Wen-Jeng Wu [1,2,6,*]. [1] *Department of Urology, School of Medicine, College of Medicine, Kaohsiung Medical University, Kaohsiung, Taiwan;* [2] *Department of Urology, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan;* [3] *Department of Urology, Ministry of Health and Welfare Pingtung Hospital, Pingtung, Taiwan;* [4] *Institute of Biomedical Sciences, National Sun Yat-Sen University, Kaohsiung, Taiwan;* [5] *Department of Urology, Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung, Taiwan;* [6] *Department of Urology, Kaohsiung Municipal Hsiao-Kang Hospital, Kaohsiung Medical University, Kaohsiung, Taiwan*

Purpose: Hepatoma-derived growth factor (HDGF) is a nucleus targeted growth factor, it has been reported to exert mitogenic effects on several types of cells and elevated in various types of cancers suggesting an important role in the development and progression of cancers. Our study was designed to elucidate the correlation of HDGF expression and prognosis in patients with upper urinary tract urothelial carcinoma (UTUC). The related mechanisms of HDGF involved were investigated using urothelial cancer cell lines.
Patients and methods: One hundred and fifty-eight UTUC specimens were analyzed for HDGF by immunohistochemistry. HDGF expression in urothelial cancer cell lines was analyzed by RT-PCR and western blotting. *In vitro* characterizations of the cellular function of recombinant HDGF in epithelial-mesenchymal transition (EMT) and tumorigenic behaviors were performed by trans-well assay and colony formation assay, respectively.
Results and conclusion: Overexpression of HDGF was present in 74 patients (46.8%). A positive HDGF expression was significantly associated with higher disease progression ($p = 0.036$) and cancer-related death rates ($p = 0.001$). In vitro study showed that overexpression of HDGF in non-invasive UC cells could significantly increase their cellular proliferation, colonies formation, and migration/invasion ability through the PI3K/AKT pathway. In contrast, knockdown of HDGF high expression UC cells with its specific shRNA inhibited the growth ability using colonies formation experiments. These results indicated that HDGF overexpression is associated with aggressive biological behavior of UC cells via the PI3K/AKT pathway. In conclusion, our study shown that HDGF is participated in UC disease progression processes. HDGF can be a potential prognostic prediction biomarker for patients with invasive UTUC post-operatively. Further identification of the molecular mechanisms involved and searching for specific targets related are warranted.

MP5-10.
LONG TERM RENAL FUNCTION FOLLOWING NEPHROURETERECTOMY IN UPPER URINARY TRACT TRANSITIONAL CELL CARCINOMA: 3 YEARS EXPERIENCE

Chan-Jung Liu, Chien-Hui Ou, Wen-Horng Yang. *National Cheng Kung University Hospital Department of Urology, Taiwan*

Purpose: This study is designed to evaluate the estimated glomerular filtration rate (eGFR) changes in patients undergoing radical nephro-ureterectomy (RNU) for upper tract urothelial carcinoma (UTUC).
Materials and methods: We retrospectively reviewed our patients with upper urinary tract TCC undergone nephroureterectomy from 2007 to 2012. Only patients with upper urinary tract transitional cell carcinoma (TCC) were enrolled in our study. We exclused the patients with end-stage-renal disease. Total 72 patients had completed follow up for three years after nephroureterectomy. The estimated glomerular filtration rate (eGFR) was calculated using the modified glomerular filtration rate estimating equation: eGFR (mL/min/1.73 m^2) = $175 \times \text{Scr}^{-1.234} \times \text{age}^{-0.179}$ ($\times$ 0.79 if female). We compared eGFR before surgery and one year after surgery, two years after surgery, and three years after surgery.
Results: Overall 72 patients were included in the study. The median age at surgery was 66.46 (46–86) years. 31 patients (44%) had a preoperative eGFR ≧ 60 mL/min per 1.73 m^2 and 53 (75%) had an eGFR ≧ 45 mL/min per 1.73 m^2. The preoperative CKD stage distribution was: CKD I ($n = 4$, 5.5%), CKD II ($n = 27$, 37.5%), CKD III ($n = 33$, 46%), and CKD IV ($n = 8$, 11.1%). After RNU, 15 patients (20.8%) had a postoperative eGFR ≧ 60 mL/min per 1.73 m^2 and 41 (56.9%) had an eGFR ≧ 45 mL/min per 1.73 m^2. The postoperative CKD stages distribution was: CKD I ($n = 1$, 1%), CKD II ($n = 14$, 19%), CKD III ($n = 46$, 64%), CKD IV ($n = 5$, 7%) and CKD V ($n = 6$, 8.3%). Comparison of preoperative and postoperative Scr levels for each patient showed a mean difference of 0.44 mg/dL ($P < 0.001$), which represents a median (IQR) increase of 27.2%. On similar analysis performed for eGFR, we found a mean difference between preoperative and postoperative eGFR of 10.8 mL/min per 1.73 m^2 ($P < 0.001$), which represents a median (IQR) decrease of 18.2 %. 3 years after RNU, 14 patients (19%) had a postoperative eGFR ≧ 60 mL/min per 1.73 m^2 and 37 (51.4%) had an eGFR ≧ 45 mL/min per 1.73 m^2. The long-term CKD stages distribution was: CKD I ($n = 0$, 0%), CKD II ($n = 14$, 19%), CKD III ($n = 38$, 53%), CKD IV ($n = 11$, 22.2%) and CKD V ($n = 9$, 12.5%). The eGFR decreased within years as 58.06, 47.28, 45.68, and 41.91 mL/min per 1.73 m^2 ($P < 0.001$).
Conclusions: TCCs located in the upper urinary tract had negative impact on the ipsilateral renal function. eGFR was relatively low and furthermore, it significantly decreased within years after RNU.

* Corresponding author.
* Corresponding author.